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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,409	06/17/2005	Reinhold Buck	08806.0179	4997

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EXAMINER	
CHRISTIAN, MARJORIE ELLEN	
ART UNIT	PAPER NUMBER
1797	
MAIL DATE	DELIVERY MODE
10/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,409	BUCK ET AL.	
	Examiner	Art Unit	
	MARJORIE CHRISTIAN	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 7/10/2009 has been entered and fully considered.

2. **Claims 1-15, 29-31** are pending and have been fully considered.

Double Patenting

3. **Claims 1-15, 29-31** are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-7 of copending Application No. 10/540,123. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both disclose a hollow fiber membrane comprising a hydrophobic and hydrophilic polymer with multiple layers.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102/103

4. **Claims 1, 7-11, 13, 26-29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 4,935,141, BUCK et al. as evidenced by US Patent No. 6,802,820, GORSUCH et al..**

As to **Claim 1**, BUCK discloses a permselective asymmetric hollow fiber membrane, comprising hydrophobic and hydrophilic polymer (Claim 1), and proteins having molecular weight of at least that of albumin are completely rejected from the membrane (C5/L46-54), where it is implicit or at least obvious that BUCK allows

passage of molecules having a molecular weight of up to 45 kDa (BUCK, Claim 1), as evidenced by GORSUCH. GORSUCH discloses the sieving co-efficients of various components based on their molecular weight in the hollow fiber membrane and that they vary from 0.1-1 in the presence of blood and water, based on multiple factors (Fig. 7). Further, it has been held that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)*.

It is inherent that the hollow fiber membrane has a molecular weight exclusion limit in water of about 200 kDa and sieving coefficient of 0.1-1.0 in the presence of blood and sieving coefficient of 0.1 in water, as evidenced by GORSUCH (Fig. 7). GORSUCH provides evidence in Fig. 7 that size exclusion limits and sieving coefficients can be easily manipulated based on the test methods used to determine the size exclusion limits and sieving coefficients; and a multitude of possible structural and operational limitations can be envisaged based on these characteristics. Therefore, many hollow fiber membranes would appear to have the desired size exclusion limit and sieving coefficients and the size exclusion limit and sieving coefficient has no limiting effect.

Alternatively, it has been held obvious to optimize a result effective variable (size exclusion limits and sieving coefficients) and BUCK discloses that size exclusion limits are result-effective variables in filtration (C5/L1-56). Therefore, the invention as a whole

would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

As to **Claim 7**, BUCK discloses a 3-layer asymmetric structure (Fig. 1a, b).

As to **Claims 8-9**, BUCK discloses a separation layer is present in the inner most layer of the hollow fiber and has a thickness of less than 1 μm (C3/L53-55, C4/L8-16), where it would be obvious to optimize the thickness of the separation layer by routine experimentation.

As to **Claim 10**, BUCK discloses the separation layer contains pore channels (Fig. 2A).

As to **Claims 11, 29**, BUCK discloses the pore size in the separation layer is 20-40 nm (Claim 2).

As to **Claim 13**, BUCK discloses the sieving coefficient for albumin in presence of whole blood is below 0.05 (C5/L46-54).

As to **Claims 26-28**, BUCK discloses hemofiltration, hemodialysis and hemofiltration of whole blood comprising filtering the blood with at least one membrane as claimed in **claim 1** (C4/6, C5/L21-23, Ex. 3).

5. **Claims 1, 3-11, 13-14, 26-29, 30 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over EP 0 568 045, KAGAWA et al. as evidenced by US Patent No. 6,802,820, GORSUCH et al..**

As to **Claims 1, 3-6, 13**, KAGAWA discloses a hollow fiber membrane with an asymmetric structure comprising: polysulfone and polyvinylpyrrolidone, with the polymer composition in the range of 90% hydrophobic and 10% hydrophilic and 60% hydrophobic and 40% hydrophilic which encompasses the claimed ranges (KAGAWA, Claim 1). KAGAWA further discloses a sieiving co-efficient of albumin less than 0.05 (Table 1), and high permeation of middle molecular weight proteins (Pg. 16, Lines 5-6) it is implicit that the membrane allows passage of molecules having a molecular weight of up to 45kDa, as evidenced by GORSUCH. GORSUCH discloses the sieving co-efficients of various components based on their molecular weight in the hollow fiber membrane (Fig. 7). Further, it has been held that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

It is inherent that the hollow fiber membrane has a molecular weight exclusion limit in water of about 200 kDa and sieving coefficient of 0.1-1.0 in the presence of blood and sieving coefficient of 0.1 in water, as evidenced by GORSUCH (Fig. 7). GORSUCH provides evidence in Fig. 7 that size exclusion limits and sieving coefficients can be easily manipulated based on the test methods used to determine the size exclusion limits and sieving coefficients; and a multitude of possible structural and operational limitations can be envisaged based on these characteristics. Therefore, many hollow fiber membranes would appear to have the desired size exclusion limit and sieving coefficients and the size exclusion limit and sieving coefficient has no limiting effect.

Alternatively, it has been held obvious to optimize a result effective variable (size exclusion limits and sieving coefficients) and KAGAWA discloses that size exclusion limits are result-effective variables in filtration (Pg. 10, Lines 52-Pg. 11, Lines 3). Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

As to **Claims 7-9, 14, 30**, KAGAWA discloses that the membrane has a three layer structure with an inner separating layer having a thickness of 0.1-3 μm (Pg. 10, Lines 44-51) and an outer pore diameter of 0.5-3 μm. KAGAWA further discloses the process conditions can be modified to optimize the outer surface structure using a spinning process whereby hollow fiber membranes having many micropores of relatively large diameter in their outer surface can be readily obtained and it would naturally flow that it has pores in the range of 20,000 to 100,000 pores per mm^2 on the outer surface, absent evidence to the contrary.

Alternatively, KAGAWA presents a finding that one of ordinary skill in the art could optimize the process conditions to obtain the desired pore size and number of pores on the surface with a reasonable expectation of success. It has been held that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

As to **Claims 10-11, 29**, KAGAWA discloses that the outer surface layer has microslits (pore channels and diameter) with width of 0.001-0.05 micron, which overlaps the range of less than 20-40nm (Pg. 10, Lines 44-51).

As to **Claims 26-28**, KAGAWA discloses that the membrane of Claim 1 is used in hemodialysis, hemofiltration and hemoconcentration (Abstract).

6. **Claims 1, 5-7, 26-28 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 6,802,820, GORSUCH et al..**

As to **Claims 1, 5-6**, GORSUCH discloses a permselective asymmetric hollow fiber membrane, comprising: polysulfone modified with polyethylene oxide- polyethylene glycol copolymer (C4/L63-65) and the membrane allows passage of molecules having a molecular weight of up to 45 kDa in presence of whole blood (Fig. 7); and that the sieving coefficient for albumin is 0.05 (Fig. 7). It is inherent that the hollow fiber membrane has a molecular weight exclusion limit in water of about 200 kDa and sieving coefficient of 0.1-1.0 in the presence of blood and sieving coefficient of 0.1 in water, as evidenced by GORSUCH (Fig. 7). GORSUCH provides evidence in Fig. 7 that size exclusion limits and sieving coefficients can be easily manipulated based on the test methods used to determine the size exclusion limits and sieving coefficients; and a multitude of possible structural and operational limitations can be envisaged based on these characteristics. Therefore, many hollow fiber membranes would appear to have the desired size exclusion limit and sieving coefficients and the size exclusion limit and sieving coefficient has no limiting effect.

Alternatively, it has been held obvious to optimize a result effective variable (size exclusion limits and sieving coefficients) “[W]here the general conditions of a claim are

disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." GORSUCH discloses that size exclusion limits and sieving coefficients are result-effective variables in filtration as shown in Fig. 7. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

As to **Claim 7**, GORSUCH discloses at least a 3-layer asymmetric structure (Claim 6).

As to **Claims 26-28**, GORSUCH discloses using the membrane of **Claim 1** to perform hemofiltration, hemodialysis and hemodiafiltration with the membrane of (C5/56-C6/L7).

7. **Claim 12 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 4,935,141, BUCK et al. as evidenced by HERBELIN et al., *Elevated circulating levels of interleukin-6 in patients with chronic renal failure*.**

As to **Claim 12**, BUCK discloses the sieving coefficients for various blood components (C5/L46-54), where it is inherent that the sieving coefficient for IL-6 in presence of whole blood is 0.9-1.0 based on the molecular weight of IL-6 (approximately 26 kDa), or it would at least be obvious to optimize the sieving coefficient of IL-6 as it is well-known that excessive amounts of IL-6 are commonly present and produced in patients receiving renal treatments and excessive amounts of IL-6 have detrimental effects, as evidenced by HERBELIN. HERBELIN discloses that

patients in chronic renal failure have elevated levels in IL-6 and that elevated levels result in an acute inflammatory response (pg. 954-960). Further, it has been held that optimization of result-effective variables is a matter of routine for a person having ordinary skill in the art and therefor is not patentably significant. Additionally, sieving coefficients can be easily manipulated based on a multitude of possible structural and operational limitations (for example ultrafiltration rate). Therefore, many hollow fiber membranes would appear to have the desired sieving coefficients and the sieving coefficient has no limiting effect.

8. **Claim 12 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over EP 0 568 045, KAGAWA et al. as evidenced by HERBELIN et al., *Elevated circulating levels of interleukin-6 in patients with chronic renal failure*.**

As to **Claim 12**, KAGAWA discloses that the hollow fiber membranes have a high sieving co-efficient for middle molecules (Pg. 16, Lines 5-6, Table 1), where it is implicit that the sieiving co-efficient for IL-6 (weight of approximately 26kDa) is 0.9-1.0. Alternatively, it would at least be obvious to optimize the sieving co-efficient of IL-6 as it is well-known that excessive amounts of IL-6 are commonly present in patients with chronic renal failure and excessive amounts of IL-6 have detrimental effects, as evidenced by HERBELIN. HERBELIN discloses that patients in chronic renal failure have elevated levels in IL-6 and that elevated levels result in an acute inflammatory response (pg. 954-960). Further, it has been held that optimization of result-effective

variables is a matter of routine for a person having ordinary skill in the art and therefor is not patentably significant. Additionally, sieving coefficients can be easily manipulated based on a multitude of possible structural and operational limitations (for example ultrafiltration rate). Therefore, many hollow fiber membranes would appear to have the desired sieving coefficients and the sieving coefficient has no limiting effect.

9. **Claim 12 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 6,802,820, GORSUCH et al. as evidenced by HERBELIN et al., *Elevated circulating levels of interleukin-6 in patients with chronic renal failure*.**

As to **Claim 12**, GORSUCH discloses the sieving coefficients in whole blood for hollow fiber membrane is based on the molecular weight of the components and as the molecular weight of IL-6 is 26kDa it appears that the sieving co-efficient for IL-6 would be 0.9-1.0. Alternatively, it would at least be obvious to optimize the sieving co-efficient of IL-6 as it is well-known that excessive amounts of IL-6 are commonly present in patients with chronic renal failure and excessive amounts of IL-6 have detrimental effects, as evidenced by HERBELIN. HERBELIN discloses that patients in chronic renal failure have elevated levels in IL-6 and that elevated levels result in an acute inflammatory response (pg. 954-960). Further, it has been held that optimization of result-effective variables is a matter of routine for a person having ordinary skill in the art and therefor is not patentably significant. Additionally, sieving coefficients can be easily manipulated based on a multitude of possible structural and operational

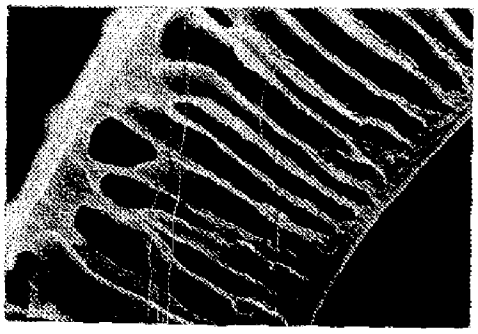
limitations (for example ultrafiltration rate). Therefore, many hollow fiber membranes would appear to have the desired sieving coefficient and the sieving coefficient has no limiting effect.

10. **Claims 14-15, 30-31 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 4,935,141, BUCK et al. as evidenced by EP 0 568 045, KAGAWA et al. and US Patent No. 6,802,820, GORSUCH et al..**

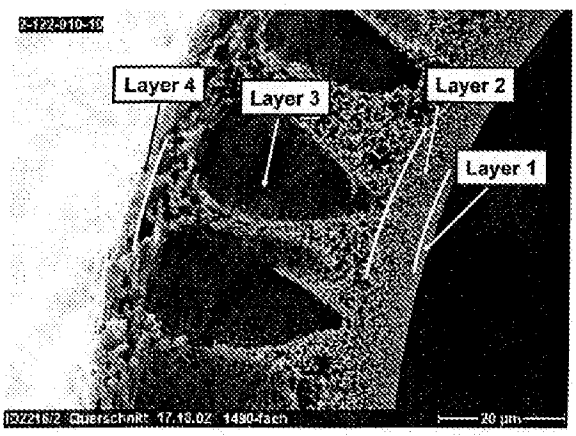
As to **Claims 14-15, 30-31**, BUCK inherently has an outer layer, different from the finger-like structure and this outer layer is equated with Applicant's fourth layer. As shown in the figures below, with prior art of BUCK on the left and the current application on the right, it is presumed that the structure of BUCK has the stated properties of an outer surface including a pore size of 0.5 to 3 micron, alternatively it would have been obvious to produce a membrane with a outer layer pore size in the range of 0.5 to 3 micron based on the teachings of BUCK which has the same sponge-like and finger-like structure of layers and the same inner layer pore size, as evidenced by KAGAWA. KAGAWA discloses that outer surface layer has micropores with a 0.1-0.5 micron average pore diameter (Pg. 10, Lines 44-51).

Further, it is either inherent or would have been obvious to produce an outer sponge layer with the property of pore density in the range of 20,000 to 100,000 pores per mm^2, based on the similarity in structure and as evidenced by KAGAWA. KAGAWA discloses the process conditions can be modified to optimize the outer surface structure

using a spinning process whereby hollow fiber membranes having many micropores of relatively large diameter in their outer surface can be readily obtained. KAGAWA presents a finding that one of ordinary skill in the art could optimize the process conditions to obtain the desired pore size and number of pores on the surface with a reasonable expectation of success.



Buck (US 4,935,141) FIG. 1b



Current Application 10/540,123 Fig. 4

Alternatively, although BUCK does not appear to expressly disclose that this outer layer is the fourth layer, it would have been obvious to one having ordinary skill in the art to include a fourth layer as it has been held that mere duplication of parts has no patentable significance. *In re Harza, 274 F.2d 669, 124 USPQ 378 (CCPA 1960)*. Including four layers in a hollow fiber membrane is well-known, as evidenced by GORSUCH. GORSUCH discloses four zones in hollow fiber membrane (Fig. 1). Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 103

11. **Claims 2-6 are rejected under 35 U.S.C. 103(a) as obvious over US Patent No. 4,935,141, BUCK et al. in view of *Blood Material interactions at the surfaces of membranes in medical applications*, DEPPISCH et al..**

As to **Claims 2-6**, BUCK discloses that the hydrophobic polymer is polysulfone, polycarbonate, or polyamide, the hydrophilic polymer is polyvinylpyrrolidone, and it appears that the hydrophobic polymer is present in the amount of 50-80% by weight, and the hydrophilic polymer is present in the amount of 20-50% by weight (Ex. 1-2,4-5, Claims 6-7, 9). BUCK does not appear to expressly disclose the size of hydrophilic domains. However it is well known, as disclosed by DEPPISCH, that PVP and PA hemodialysis membranes have hydrophilic domains in the range of 20-200 nm (Pg. 247, Col. 2, Para. 1) and that hydrophilic domains improve thrombogenicity (Pg. 248, Col. 2, Lines 1-4). Since, DEPPISCH recognizes hydrophilic domains as a result effective variable and it would be obvious to a person having ordinary skill in the art to optimize the size of the domains as it has been held that it is not inventive to discover the optimum ranges by routine experimentation. *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).*

12. **Claims 2-6 are rejected under 35 U.S.C. 103(a) as obvious over 0 568 045, KAGAWA et al. in view of *Blood Material interactions at the surfaces of membranes in medical applications*, DEPPISCH et al..**

As to **Claims 2-6**, discloses a hollow fiber membrane with an asymmetric structure comprising: polysulfone and polyvinylpyrrolidone, with the polymer composition in the range of 90% hydrophobic and 10% hydrophilic and 60% hydrophobic and 40% hydrophilic which encompasses the claimed ranges (KAGAWA, Claim 1). KAWAGA does not appear to expressly disclose the size of hydrophilic domains. However it is well known, as disclosed by DEPPISCH, that PVP and PA hemodialysis membranes have hydrophilic domains in the range of 20-200 nm (Pg. 247, Col. 2, Para. 1) and that hydrophilic domains improve thrombogenicity (Pg. 248, Col. 2, Lines 1-4). Since, DEPPISCH recognizes hydrophilic domains as a result effective variable and it would be obvious to a person having ordinary skill in the art to optimize the size of the domains as it has been held that it is not inventive to discover the optimum ranges by routine experimentation.

Response to Arguments

13. Applicant's arguments filed 7/10/2009 have been fully considered but they are not persuasive in view of the new grounds of rejection.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARJORIE CHRISTIAN whose telephone number is (571)270-5544. The examiner can normally be reached on Monday through Thursday 7-5pm (Fridays off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Krishnan S Menon/
Primary Examiner, Art Unit 1797

MC